IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF
ROBERT J. PEACH ET AL.
PATENT NO: 7,094,874
ISSUED: AUGUST 22, 2006
FOR: SOLUBLE CTLA4 MUTANT MOLECULES AND USES THEREOF

FILING VIA EFS-WEB
Mail Stop: PETITIONS
Director, U.S. Patent & Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO DECISION ON REQUEST FOR RECONSIDERATION OF PATENT TERM ADJUSTMENT

Sir:

The Office of Petitions issued a *Decision on Request for Reconsideration of Patent Term Adjustment* ("Decision")[1] that erroneously reduced the term of U.S. Patent 7,094,874 by 81 days. The Decision, dated February 21, 2007, alleged that while prosecuting the patent, the applicants filed a "reply having an omission" that triggers a reduction of patent term adjustment under 37 C.F.R. § 1.704(c)(7). To the contrary, the filing was complete and does not implicate 37 C.F.R. § 1.704(c)(7). Thus, the Director should correct the patent term adjustment by adding 81 days back to the patent term adjustment period. Upon correction, the total patent term adjustment period will be 261 days.

The Filing was Complete

The filing at issue ("Filing")[2] was a Request for Continued Examination (RCE), accompanied by a Response that included claim amendments, made on October 24, 2005. According to the Decision, the Filing had an omission that prompted the examiner to mail a

[1] A copy of the Decision is attached as Appendix A.
[2] A copy of the Filing is attached as Appendix B.

Notice of Non-Compliant Amendment ("Notice")[3] on November 14, 2005. The Notice alleged that the Filing violated 37 C.F.R. § 1.121 because "multiple dependent claims cannot depend on other multiple dependent claims," but the Notice was unwarranted. The mere presence of improper multiple dependent claims is not non-compliance with 37 C.F.R. § 1.121, nor is it a basis for alleging that the Filing was incomplete.

Rule 37 C.F.R. § 1.121 governs the manner of making amendments in an application. It establishes the following requirements for claim amendments:

(a) The paper on which claim amendments are presented must comply with format requirements set forth in 37 C.F.R. § 1.52 (*e.g.*, size of paper, margins, line spacing, *etc.*);

(b) A complete listing of the claims must be presented on pages separate from other portions of the document containing them;

(c) The claims must be presented in ascending order;

(d) Appropriate status identifiers must be used for the claims; and

(e) All claims must be written in their entirety, with any additions and deletions indicated by appropriate markings, except when a claim is canceled.

The Filing met all of those requirements (and any others actually specified by 37 C.F.R. § 1.121 for claims). The examiner never alleged otherwise.

Additionally, the Filing complied with the *purpose* of 37 C.F.R. § 1.121, which exists to facilitate examination of patent applications. A multiple dependent claim that depends from another multiple dependent claim does not impede the examination of an application. Indeed, MPEP § 608.01(n) provides patent examiners with a straightforward way to address such claims. It instructs them that "[a] multiple dependent claim which depends from another multiple dependent claim should be objected to by using form paragraph 7.45." That form paragraph reads as follows:

> *Claim [X] is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.*

[3] A copy of the Notice is attached as Appendix C.

Because such a straightforward way of dealing with multiple dependent claims in the Filing existed, their presence did not complicate the examination process and was not a proper basis for issuing the Notice.

Beyond the multiple dependent claims, the examiner alleged no other basis for the Notice. Nevertheless, it is noteworthy that the Filing contained a complete reply to the examiner's previous Office Action, as required by 37 C.F.R. § 1.114(c). Specifically, the Response portion of the Filing addressed every outstanding rejection and/or objection lodged against the application. The examiner never alleged otherwise.

The Director Should Correct the Patent Term Adjustment Period

Because the Filing was complete, the Director should add 81 days back to the patent term adjustment period. Reductions in patent term adjustment apply only when applicants "fail[ ] to engage in reasonable efforts to conclude prosecution (processing or examination) of the application." 37 C.F.R. § 1.704(a). The Patent Office has described such circumstances in terms of "actions or inactions by an applicant that interfere with the Office's ability to process or examine an application." As explained above, such circumstances do not apply to the Filing.

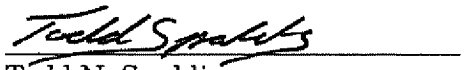
This Response is Timely

As this response is being filed within two months of the Decision being mailed, it is timely.

Payment of Any Required Fees

If any fees are required for consideration of this response, please charge them to Deposit Account No. 19-3880 in the name of Bristol-Myers Squibb Company.

Respectfully submitted,



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Date: April 19, 2007

Appendix A -

Decision on Request for Reconsideration of Patent Term Adjustment

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
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Paper No.

LOUIS J. WILLE
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FEB 2 1 2007

OFFICE OF PETITIONS

In re Patent No. 7,094,874	:	DECISION ON REQUEST
Peach et al.	:	FOR RECONSIDERATION OF
Issue Date: August 22, 2006	:	PATENT TERM ADJUSTMENT
Application No. 09/865,321	:	and
Filed: May 23, 2001	:	NOTICE OF INTENT TO ISSUE[1]
Atty Docket No. D0028PNP; 30436.57USU1	:	CERTIFICATE OF CORRECTION

This is a decision on the "APPLICATION TO CORRECT PATENT TERM ADJUSTMENT PERIOD IN GRANTED PATENT UNDER 37 C.F.R. §§ 1.181 & 1.705" filed October 20, 2006, which is properly treated pursuant to 37 CFR 1.705(d). Patentees request that the revised Patent Term Adjustment shown on the above captioned patent be corrected from two hundred fifty-three (253) days to three hundred sixty-five (365) days.

The request for reconsideration of the patent term adjustment indicated in the patent is **GRANTED to the extent indicated herein**.

Patentees are given **TWO (2) MONTHS** from the mail date of this decision to respond. No extensions of time will be granted under § 1.136.

For the reasons stated herein, the patent term adjustment indicated in the patent is to be corrected by issuance of a

certificate of correction showing a revised Patent Term Adjustment of **ONE HUNDRED EIGHTY (180)** days.

On August 22, 2006, the above-identified application matured into U.S. Patent No. 7,094,874. The instant request for reconsideration filed October 20, 2006 was timely filed within 2 months of the date the patent issued. See § 1.705(d). The Patent issued with a revised Patent Term Adjustment of 253 days. Patentees dispute the reductions, pursuant to 37 CFR 1.704(c)(10), of 8, 29, and 75 days respectively for the filing of a supplemental Application Data Sheet (ADS) on April 20, 2006, Drawings on May 11, 2006 and Drawings on June 9, 2006. Patentees do not dispute that these papers were filed after the mailing of the notice of allowance. Rather, patentees argue that: The Office improperly charged Applicants with 8 days of delay for filing a supplemental ADS that the Office itself requested. The Office erroneously charged Applicants with 29 days of delay for filing a first corrected drawing, when Applicants had no warning before the Notice of Allowance that corrected drawings would be necessary. The Office incorrectly charged Applicants with 75 days of delay for filing a second set of corrected drawings, again when Applicants had no warning before the Notice of Allowance that corrected drawings would be necessary.

Patentees' arguments have been considered. With respect to the reductions associated with the filing of drawings after the mailing of the notice of allowance, patentees' arguments are not persuasive. Patentees acknowledge submitting drawings after the mailing of the notice of allowance. Patentees are advised that the filing of drawings after the mailing of a notice of allowance is properly a basis for reduction of patent term adjustment.

37 CFR § 1.704(c)(10) provides that:

Submission of an amendment under § 1.312 or other paper after a notice of allowance has been given or mailed, in which case the period of adjustment set forth in § 1.703 shall be reduced by the lesser of:

> (i) The number of days, if any, beginning on the date the amendment under § 1.312 or other paper was filed and ending on the mailing date of the Office action or notice in

response to the amendment under § 1.312 or such other paper;

or

(ii) Four months;

In this instance, it is undisputed that the drawings were filed after the mailing of the notice of allowance. Accordingly, pursuant to § 1.704(c)(10), the patent term adjustment was properly reduced by 29 days for the drawings filed May 11, 2006 (for the period beginning on May 11, 2006 and ending on June 8, 2006, the day before further drawings were filed) and by 75 days for the drawings filed June 9, 2006 (for the period beginning on June 9, 2006 to the issuance of the patent on August 22, 2006). (The first period ended on June 8, 2006 so as not to overlap with the second period of reduction for drawings).

As stated in MPEP 2732, by Notice entitled Clarification of 37 CFR 1.704(c)(10) - Reduction of Patent Term Adjustment for Certain Types of Papers Filed After a Notice of Allowance, 1247 OG 111 (June 26, 2001), the Director set forth examples of papers deemed not to cause substantial interference and delay in the patent issue process. A submission of drawings was not identified in the Notice. Other than those papers identified in this Notice, all papers filed after allowance of an application substantially delay the Office's ability to process an application for a patent because the Office does not wait until payment of the Issue Fee to begin the patent issue process. As a result, 37 CFR 1.704(c)(10) does not distinguish between papers that are and are not required by the Office. Filing of any drawings after allowance will be treated as a failure to engage in reasonable efforts to conclude prosecution.

Furthermore, it is noted that corrected drawings were required because the drawings originally filed by applicants were inconsistent with their own Brief Description of Drawings. Thus, applicants did not have to wait until the mailing of a notice to be aware of and take action to correct this inconsistency. Further, the second filing of drawings after the mailing of the notice of allowance was required because of the quality of the earlier filed set of drawings filed. The drawings filed June 9, 2006 are of a better quality than the drawings previously-filed. Applicants were not precluded from submitting better quality drawings earlier.

However, with respect to the reduction of 8 days associated with the supplemental ADS filed April 20, 2006, Patentees' contention is well taken. The record supports a conclusion that by amendment filed March 3, 2003, the requested correction to the priority claim was entered in the application. This was well before the mailing of the notice of allowance on March 21, 2006. At the request of the examiner, this information was resubmitted in the form of a supplemental ADS on April 20, 2006. It is not controlling that the ADS was requested by the examiner. Rather, given that the ADS was, in effect, a resubmission of a previously-filed paper and under the circumstances of this case, it is appropriate to treat the ADS for purposes of PTA calculation as submitted by way of an amendment on March 3, 2003, prior to the mailing of the notice of allowance on March 21, 2006. Thus, the resubmission of the amendment by way of an ADS on April 20, 2006 did not constitute a failure to engage within the meaning of 37 CFR 1.704(c)(10). The reduction of 8 days is removed.

However, the review of the reduction reveals a further basis for entry of a period of reduction. Specifically, on October 24, 2005, applicants filed a Request for Continued Examination and an amendment. By Notice mailed November 14, 2005, applicants were advised of an omission in this response. On January 13, 2006, applicants filed a response correcting the omission. 37 CFR 1.704(c)(7) provides that "Submission of a reply having an omission (§1.135(c))," is a "failure to engage" and that "the period of adjustment set forth in § 1.703 shall be reduced by the number of days, if any, beginning on the day after the date the reply having an omission was filed and ending on the date that the reply or other paper correcting the omission was filed." Accordingly, pursuant to this section, a period of reduction of 81 days is being entered for the period from October 25, 2005 to January 13, 2006.

In view thereof, the patent term adjustment indicated on the patent should be one hundred eighty (180) days.

The Office acknowledges submission of the $200.00 fee set forth in 37 CFR 1.18(e). No additional fees are required.

The application file is being forwarded to the Certificates of Correction Branch for issuance of a certificate of correction in order to rectify this error. The Office will issue a

certificate of correction indicating that the term of the above-identified patent is extended or adjusted by ONE HUNDRED EIGHTY (180) days.

Telephone inquiries specific to this matter should be directed to the undersigned at (571) 272-3219.

Nancy Johnson
Senior Petitions Attorney
Office of Petitions

Enclosure: Copy of DRAFT Certificate of Correction

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT : 7,094,874 B2

DATED : August 22, 2006

INVENTOR(S) : Peach et al.

DRAFT

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the cover page,

[*] Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 USC 154(b) by (253) days

Delete the phrase "by 253" and insert – by 180 days--

Appendix B -

Request for Continued Examination (Including Response)

PTO/SB/30 (04-05)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Request for Continued Examination (RCE) Transmittal

Address to:
Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Application Number	09/865,321
Filing Date	5/23/2001
First Named Inventor	ROBERT PEACH
Art Unit	1644
Examiner Name	OUSPENSKI, ILIA I
Attorney Docket Number	D0028 NP

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. See Instruction Sheet for RCEs (not to be submitted to the USPTO) on page 2.

1. Submission required under 37 CFR 1.114 Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

   a. ☐ *Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.*

      i. ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____

      ii. ☐ Other _____

   b. ☑ Enclosed

      i. ☑ *Amendment/Reply*

      ii. ☐ Affidavit(s)/ Declaration(s)

      iii. ☑ *Information Disclosure Statement (IDS)*

      iv. ☑ Other 1449 Forms

2. Miscellaneous

   a. ☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of _____ months. (Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)

   b. ☐ Other _____

3. Fees The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.

   a. ☑ The Director is hereby authorized to charge the following fees, any underpayment of fees, or credit any overpayments, to Deposit Account No. 19-3880. I have enclosed a duplicate copy of this sheet.

      i. ☑ RCE fee required under 37 CFR 1.17(e)

      ii. ☑ Extension of time fee (37 CFR 1.136 and 1.17)

      iii. ☑ Other Extra Claim Fee Letter

   b. ☐ Check in the amount of $ _____ enclosed

   c. ☐ Payment by credit card (Form PTO-2038 enclosed)

WARNING: *Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.*

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

Signature	Audrey F. Sher			Date	October 21, 2005
Name (Print/Type)	Audrey F. Sher	Phone	609-252-3218	Registration No.	39,024

CERTIFICATE OF MAILING OR TRANSMISSION

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450 or facsimile transmitted to the U.S. Patent and Trademark Office on the date shown below.

Signature	Audrey F. Sher		
Name (Print/Type)	Audrey F. Sher	Date	October 21, 2005

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Audrey F. Sher		October 21, 2005
Type or print name	Signature	Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

Robert J. Peach et al.

APPLICATION NO: 09/865,321

FILED: May 23, 2001

FOR: SOLUBLE CTLA4 MUTANT MOLECULES AND USES THEREOF

Art Unit: 1646

Examiner: Ilia Ouspenski

Mail Stop **RCE**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Response

Sir:

This Communication is contemporaneously submitted with a Request for Continued Examination in response to the Final Office Action dated September 27, 2004 and the Advisory Action dated January 10, 2005 issued by the U.S. Patent & Trademark Office in connection with the above-identified application.

Amendments to the claims are reflected in the listing of claims which begin on page 2 of the paper.

Remarks/Arguments begin on page 8 of this paper.

In the claims:

This listing of claims will replace all prior versions, and listings, of claims in the application. Please amend claims 70, 78, 95, 96 and 114 as follows. Please add new claims 116-119 as follows.

Listing of Claims:

--1 to 66. (Cancelled)

--67. (Previously Presented) A CTLA4 mutant molecule which binds CD80 and/or CD86 comprising an extracellular domain of CTLA4 as shown in SEQ ID NO:8 beginning with alanine at position 26 or methionine at position 27 and ending with aspartic acid at position 150, or a portion thereof, wherein in the extracellular domain or portion thereof an alanine at position 55 is substituted with a tyrosine, and a leucine at position 130 is substituted with a glutamic acid. --

--68. (Previously Presented) A CTLA4 mutant molecule comprising:

(a) an amino acid sequence beginning with methionine at position 27 and ending with aspartic acid at position 150 of SEQ ID NO:4, or

(b) an amino acid sequence beginning with alanine at position 26 and ending with aspartic acid at position 150 of SEQ ID NO:4. --

--69. (Previously Presented) A CTLA4 mutant molecule comprising:

(a) an amino acid sequence beginning with methionine at position 27 and ending with aspartic acid at position 150 of SEQ ID NO:4 or a portion thereof that binds CD80 and/or CD86, or

(b) an amino acid sequence beginning with alanine at position 26 and ending with aspartic acid at position 150 of SEQ ID NO:4 or a portion thereof that binds CD80 and/or CD86. --

--70. (Currently Amended) The CTLA4 mutant molecule of claim 67, 68, or 69 further comprising an amino acid sequence which alters the solubility or affinity of the ~~soluble~~ CTLA4 mutant molecule. --

-- 71. (Previously Presented) The CTLA4 mutant molecule of claim 70, wherein the amino acid sequence which alters the solubility or affinity comprises an immunoglobulin. --

--72. (Previously Presented) The CTLA4 mutant molecule of claim 71, wherein the immunoglobulin is an immunoglobulin constant region or portion thereof. --

--73. (Previously Presented) The CTLA4 mutant molecule of claim 72, wherein the immunoglobulin constant region or portion thereof is mutated to reduce effector function. --

--74. (Previously Presented) The CTLA4 mutant molecule of claim 72 or 73, wherein the immunoglobulin constant region comprises a hinge, CH2 and CH3 regions of an immunoglobulin molecule. --

--75. (Previously Presented) The CTLA4 mutant molecule of claim 72, wherein the immunoglobulin constant region or portion thereof is a human or monkey immunoglobulin constant region. --

--76. (Previously Presented) A CTLA4 mutant molecule comprising:

(a) an amino acid sequence beginning with methionine at position 27 and ending with lysine at position 383 of SEQ ID NO:4, or

(b) an amino acid sequence beginning with alanine at position 26 and ending with lysine at position 383 of SEQ ID NO:4. --

--77. (Previously Presented) A CTLA4 mutant molecule consisting of:

(a) an amino acid sequence beginning with methionine at position 27 and ending with lysine at position 383 of SEQ ID NO:4, or

(b) an amino acid sequence beginning with alanine at position 26 and ending with lysine at position 383 of SEQ ID NO:4. --

--78. (Currently Amended) The CTLA4 mutant molecule of claim 67, 68, 69, or 76 further comprising an amino acid sequence which permits secretion of the ~~soluble~~ CTLA4 mutant molecule. --

--79. (Previously Presented) The CTLA4 mutant molecule of claim 78, wherein the amino acid sequence which permits secretion comprises an oncostatin M signal peptide. --

--80. (Previously Presented) A CTLA4 mutant molecule comprising an amino acid sequence beginning with methionine at position 1 and ending with lysine at position 383 of SEQ ID NO:4. --

--81. (Withdrawn) A nucleic acid molecule encoding the soluble CTLA4 mutant molecule of claim 67, 68, 69, 76, 77 or 80. --

--82. (Withdrawn) The nucleic acid molecule of claim 81 comprising:

(a) the nucleic acid molecule beginning with adenine at position 79 and ending with thymine at position 450 of SEQ ID NO:3, or

(b) the nucleic acid molecule beginning with guanine at position 76 and ending with thymine at position 450 of SEQ ID NO:3. --

--83. (Withdrawn) The nucleic acid molecule of claim 81 comprising:

(a) the nucleic acid molecule beginning with adenine at position 79 and ending with adenine at position 1149 of SEQ ID NO.: 3, or

(b) the nucleic acid molecule beginning with guanine at position 76 and ending with adenine at position 1149 of SEQ ID NO:3. --

--84. (Withdrawn) The nucleic acid molecule of claim 81 comprising the nucleic acid molecule beginning with adenine at position 1 and ending with adenine at position 1149 of SEQ ID NO.: 3. --

--85. (Withdrawn) A DNA molecule encoding a soluble CTLA4 mutant molecule, wherein the DNA molecule is deposited as ATCC No. PTA-2104. --

--86. (Previously Presented) A CTLA4 mutant molecule encoded by the nucleic acid molecule designated ATCC No. PTA-2104. --

--87. (Withdrawn) A vector comprising the nucleic acid molecule of claim 81. --

--88. (Withdrawn) A vector comprising the DNA molecule of claim 85. --

--89. (Withdrawn) A vector encoding a soluble CTLA4 mutant molecule and deposited with the ATCC as ATCC No. PTA-2104. --

--90. (Withdrawn) A host cell having the vector of claim 87, 88, or 89. --

--91. (Withdrawn) The host cell of claim 90 which is a bacterial or eukaryotic cell. --

--92. (Withdrawn) The host cell of claim 91, wherein the eukaryotic cell is a COS cell or a Chinese Hamster Ovary (CHO) cell. --

--93. (Withdrawn) A method for producing a soluble CTLA4 mutant molecule comprising growing the host cell of claim 90 so as to produce the soluble CTLA4 mutant molecule in the host cell, and recovering the molecule so produced. --

--94. (Cancelled)

--95. (Currently Amended) A CTLA4 mutant molecule comprising the entire extracellular domain of the ~~soluble~~ CTLA4 mutant molecule encoded by the nucleic acid molecule designated ATCC No. PTA-2104. --

--96. (Currently Amended) A pharmaceutical composition comprising a CTLA4 mutant molecule of claim 67, 68, 69, 74, 76, 77, 86, or 95 and a pharmaceutically acceptable carrier. --

--97 to 103. (Cancelled)

--104. (Previously Presented) The CTLA4 mutant molecule of claim 71, wherein the immunoglobulin comprises a hinge and any or all of the cysteine residues within the hinge are substituted with serine. --

--105. (Previously Presented) The CTLA4 mutant molecule of claim 104, wherein a cysteine at position +156 is substituted with a serine, a cysteine at position +162 is substituted with a serine, and a cysteine at position +165 is substituted with a serine, as shown in SEQ ID NO:4. --

--106. (Previously Presented) The CTLA4 mutant molecule of claim 72, wherein the immunoglobulin constant region or portion thereof is mutated to include a cysteine at position +156 substituted with a serine, a cysteine at position +162 substituted with a serine, a cysteine at position +165 substituted with a serine, and a proline at position +174 substituted with serine, as shown in SEQ ID NO:4. --

--107. (Previously Presented) The CTLA4 mutant molecule of claim 71, wherein the immunoglobulin comprises an amino acid sequence which begins with glutamic acid at position +152 and ends with lysine at position +383, as shown in SEQ ID NO:4. --

--108. (Previously Presented) The CTLA4 mutant molecule of claims 67, 68, or 69, further comprising a junction amino acid residue and an immunoglobulin, where the

junction amino acid residue is located between the amino acid sequence which ends with aspartic acid at position +150 and the immunoglobulin. --

--109. (Previously Presented) The CTLA4 mutant molecule of claim 108, wherein the junction amino acid residue is glutamine. --

--110 to 112. (Cancelled)

-- 113. (Previously Presented) The CTLA4 mutant molecule of claims 67, 68, 69, 76 or 77, that has a slower dissociation rate from binding CD86 than wild type CTLA4. --

-- 114. (Currently Amended) The CTLA4 mutant molecule of claims 67, 68, 69, 74, 76, 77, 86, or 95, that is soluble. --

-- 115. (Cancelled)

-- 116. (New) The CTLA4 mutant molecule of claims 67, 68, 69, 74, 76, 77, 86, or 95, that is substantially pure. --

-- 117. (New) The CTLA4 mutant molecule of claims 67, 68, 69, 74, 76, 77, 86, or 95, wherein the CTLA4 mutant molecule is a dimer. --

-- 118. (New) The CTLA4 mutant molecule of claims 67, 68, 69, 74, 76, 77, 86, or 95, wherein the CTLA4 mutant molecule has a molecular mass of about 100 kilodaltons. --

-- 119. (New) The CTLA4 mutant molecule of claim 118, wherein the molecular mass is assessed by SDS-PAGE under non-reducing conditions.

Remarks

Claims 1-66, 94, 97-103, 110-112 and 115 have been cancelled previously. Claims 81-85 and 87-93 have been withdrawn.

Claims 67-69, 71-77, 79-80, 86, 104-109, and 113 have been previously presented. Claims 70, 78, 95, 96 and 114 are currently amended herein. Claims 116-119 are newly added herein. Thus claims 67-80, 86, 95, 96, 104-109, 113, 114 and 116-119 are being examined in the instant application.

The changes in the currently amended claims 70, 78, 95, 96 and 114 do not involve new matter, and are supported by the specification as originally filed. Applicants have removed the word "soluble" from claims 70, 78,and 95 because it is unnecessary for patentability. Applicants do not intend to surrender the subject matter claimed therein that is soluble.

Support for newly added claim 116 can be found on page 27 lines 12-17 of the specification as originally filed.

Support for newly added claim 117 can be found on page 36 line 26 through page 37 line 14 of the specification as originally filed.

Support for newly added claim 118 can be found on page 35 line 24 through page 36 line 1 of the specification as originally filed.

Support for newly added claim 119 can be found on page 35 line 24 through page 36 line 1 of the specification as originally filed.

Claims 67-80, 86, 95, 96, 104-109, 113 and 114 are rejected under 35 USC 102(b) as being anticipated by Peach et al. (WO 98/33513) as evidenced by Cohen et al. (US 2003/0083246).

Applicants traverse the rejection for the reasons of record. For the Examiner's convenience Applicants restate below, under the heading A., the arguments made in their response of November 29, 2004. Further below, under the heading B., Applicants provide new response not found in the response of November 29, 2004.

A. Restatement of response of November 29, 2004

The Patent Office acknowledges, on page 4 of the Office Action, "that WO98/33513 teaches that the sequence of LEA29Y is set forth in SEQ ID NO:1 (where Xaa is "Y" and Yaa is "E"), and that the amino acid sequence of SEQ ID NO:1 is not the same as instant SEQ ID NO:4 or the amino acid sequence set forth in instant Figure 7." The Applicants agree with the Patent Office and assert that Peach et al. (WO 98/33513), alone or as evidenced by Cohen et al., does not expressly or inherently anticipate the instantly claimed CTLA4 mutant molecules.

The Patent Office expresses concerns about the identity of the instantly claimed invention, relating to how the instantly claimed invention and a molecule in Peach et al. (WO 98/33513) have been named. Before directly addressing these concerns, the Applicants wish to direct the Patent Office to the claims being examined in the instant application. These claims, along with the disclosure in WO 98/33513, must drive the novelty analysis.

Each claim being examined in the instant application refers to a disclosed amino acid sequence and defines the CTLA4 mutant molecule being claimed by that amino acid sequence. In each claim, the claimed CTLA4 mutant molecule has two mutations in the CTLA4 extracellular domain relative to the wild type CTLA4 extracellular domain: a mutation of leucine at position 104 to glutamic acid; and a mutation of alanine at position 29 to tyrosine (using the numbering system of Figure 7 of the instant application). No claim claims a CTLA4 mutant molecule defined by a name. The term "LEA29Y" is not used in any claim. The claims clearly define the invention being claimed, and that definition is by sequence.

The Patent Office states, on page 3 of the Office Action, that "[n]o objective evidence that the LEA29Y molecule taught by Peach et al. is different [from] the instantly claimed LEA29Y molecule has been presented by the Applicant," and that "[a]bsent any factual evidence to clarify the identity of the claimed molecule, the [102(b)] rejection is maintained essentially for the reasons of record." The Applicants submit that the sequence in the instant application *is the evidence* defining an instantly claimed CTLA4 mutant molecule, and that the sequence *is the identity* of a claimed CTLA4 mutant molecule. There is no clarification needed. The Applicants submit that, equally importantly, the sequence in the

prior art reference WO98/33513 is the evidence defining a molecule in that prior art reference. To anticipate an instantly claimed molecule which is defined by sequence, a prior art molecule must have the same sequence as the instantly claimed molecule. As noted by the Patent Office, the sequences of the instantly claimed CTLA4 mutant molecules are not in the prior art of record.

The Applicants direct the Patent Office to SEQ ID NO:4 and Figure 7 of the instant application for clear factual evidence of the identity of a claimed CTLA4 mutant molecule comprising an amino acid sequence beginning with methionine at position 27 and ending with lysine at position 383 of SEQ ID NO:4 or an amino acid sequence beginning with alanine at position 26 and ending with lysine at position 383 of SEQ ID NO:4 (claim 76). Using the numbering system of Figure 7 of the instant application, this instantly claimed CTLA4 mutant molecule has a mutation of leucine at position 104 to glutamic acid, and a mutation of alanine at position 29 to tyrosine. To the contrary, using the same numbering system of Figure 7 of the instant application, the prior art Peach et al. (WO98/33513) discloses a CTLA4 mutant molecule which has a mutation at position 105 to glutamic acid, and a mutation at position 28 to tyrosine. The disclosure of the prior art reference does not contain each element of the sequence of the instantly claimed molecule and, therefore, cannot be anticipatory. ("Anticipation requires the presence in a single prior art reference disclosure of each and every element of the claimed invention, arranged as in the claim." *Lindermann Maschinenfabrik GMBH v. American Hoist & Derrick*, 221 USPQ 481, 485 (Fed. Cir. 1984)). Applicants assert that the instantly claimed molecules meet the legal standard for novelty.

The Patent Office, on page 3 of the Office Action, expresses confusion with the concept that a molecule can be referred to by the same name as another molecule with a different amino acid sequence. The Patent Office is unclear about how two different disclosed sequences in two different documents ended up with the same name and wishes to determine "which of the two definitions of molecular identity is correct: either (a) the same molecule is disclosed as having two different amino acid sequences in Peach et al. (WO 98/33513) and the instant application, e.g. due to a sequencing error, or (b) two different molecules have been given the same name by the same group of Inventors."

The Applicants respectfully submit that determining which of the two sequences "correctly" defines "LEA29Y" is irrelevant in determining the novelty of the instantly claimed invention. What is relevant in determining the novelty of the instantly claimed invention is what sequence was disclosed in the prior art reference and what sequence is now being claimed. A name used to refer to an invention is not important; it is the elements of the claimed invention and not the given name that defines the claimed invention. (*See, eg., Ethyl Molded Products Company v. Betts Packaging, Inc*, 9 U.S.P.Q.2D 1001, 1011 (1988) "In viewing the prior art, as well as determining infringement, the names given to parts of a closure are not important.... Thus, it is the actual structure and function of a closure part that is important, and not the name given to it by the defendant.") Sequence defines a claimed CTLA4 mutant molecule, and, as acknowledged by the Patent Office, the prior art sequence set forth in SEQ ID NO:1 of WO98/33513 is not the same as the claimed molecule defined by instant SEQ ID NO:4 or Figure 7. Applicants assert that the instantly claimed molecules meet the legal standard for novelty.

The Patent Office states, on page 4 of the Office Action that an ordinary artisan at the time of the invention would have recognized that there was a discrepancy between the sequences set forth in SEQ ID NO:1 and Figure 7 of WO98/33513 and the description of the positions mutated in the CTLA4 sequence provided on page 19 of WO98/33513. To support this assertion, the Patent Office states that "[f]or example, page 19 identifies the CDR1 loop of CTLA4 as S25 to R33, whereas Figure 7 has S26 and R34." The Patent Office seems to be asserting that because of this alleged discrepancy the instantly claimed invention was disclosed in WO98/33513 to the ordinary artisan. Without commenting on whether the ordinary artisan would indeed have recognized the alleged discrepancy, the Applicants respectfully disagree with the Patent Office's basis for the rejection.

The Patent Office refers to an alleged discrepancy in WO98/33513 in the identification of the CDR1 loop, presumably relating to the mutation at position 29 from alanine to tyrosine in the instantly claimed invention. The instantly claimed invention has two mutations: one at position 29, which is in the CDR1 loop; and one at position 104, which is not in the CDR1 loop. The rejection does not address the mutation at position 104. A proper rejection addresses all elements of the claimed invention. The Applicants submit that this rejection is inadequate because all elements of the claimed invention are

not addressed. The Applicants assert that the instantly claimed molecules meet the legal standard for novelty.

B. New response

Applicants submit concurrently herewith an Information Disclosure Statement and direct the Examiner's attention to this Information Disclosure Statement and the Information Disclosure Statements submitted on June 19, 2001, January 18, 2002, March 6, 2002, May 1, 2002, June 7, 2002, November 4, 2002, June 23, 2003. Applicants and the undersigned attorney recognize their duty of disclosure under 37 C.F.R. §1.56 and submit and have submitted the aforementioned Information Disclosure Statements in accordance with that duty.

Applicants thank the Examiner for discussing this case with the undersigned attorney. Based on Applicants' understanding of the Examiner's concerns expressed in the discussion, and based on the Office Action dated September 27, 2004, Applicants provide the following.

It is clear that the *document* Peach et al. (WO 98/33513) as evidenced by the *document* Cohen et al. (US 2003/0083246) does not anticipate the claimed invention. The claimed invention simply is not disclosed on the printed pages of Peach et al. (WO 98/33513), either alone or as evidenced by Cohen et al. (US 2003/0083246). The Office recognizes this, as it states on page 4 of the Office Action "[t]he Examiner acknowledges that WO98/33513 teaches that the sequence of LEA29Y is set forth in SEQ ID NO:1 (where Xaa is "Y" and Yaa is "E"), and that the amino acid sequence of SEQ ID NO:1 is not the same as instant SEQ ID NO:4 or the amino acid sequence set forth in instant Figure 7."

Although recognizing that the claimed invention is not anticipated by the disclosures on the printed pages of the cited reference documents, the Office takes a step away from those disclosures and tries to read between the lines of the cited references, attempting to glean from the cited references when a physical embodiment of the claimed invention may have existed. The claimed invention could have existed before the priority dates, the Office imagines. The Office then takes another step that completely exits the realm of the cited reference documents. The Office hypothesizes that if a physical embodiment of the claimed invention existed before the priority dates, it or a description of it may have left the

control of the inventors and been publicly available before the priority dates -- through some means other than the clearly unanticipatory cited references.

It must be recognized that nowhere on the printed pages of Peach et al. (WO 98/33513) or Cohen et al. (US 2003/0083246) does it say or even suggest that a physical embodiment of the instantly claimed invention, or a description of it, (or, for that matter, of the invention described in Peach et al. (WO 98/33513)) was made publicly available. Thus any rejection brought concerning public availability of the claimed invention is not properly brought over the cited references.

Applicants confirm that they produced and had possession of a physical embodiment of a molecule covered by at least one claim of the instant application before the priority dates of the instant application. This is clearly evidenced in the Information Disclosure Statements.

However, it does not follow from the above facts that the claimed invention was publicly available before the priority dates of the instant application. Existence is not equal to public availability, and existence is not a bar to patentability.

Many, if not most, patent applications are filed after the applicant has produced a physical embodiment and is in possession of the claimed invention. The Examples of countless patent applications claiming compound X make clear that compound X was produced before the priority date. With respect to all such patent applications, the Office could hypothesize that the applicant may have made the claimed invention publicly available before the priority date. The law provides 37 C.F.R. §1.56 to address that hypothesis. The duty under 37 C.F.R. §1.56 ensures that the Office will be made aware of all information known to each individual associated with the filing and prosecution of the patent application to be material to patentability. In response to the Office's hypothesis, the applicant need do nothing more than meet its duty under 37 C.F.R. §1.56. This seems only fair, since the Office's hypothesis is just that – an hypothesis, unsubstantiated speculation.

Applicants submit concurrently herewith an Information Disclosure Statement and direct the Examiner's attention to this Information Disclosure Statement and the Information Disclosure Statements submitted on June 19, 2001, January 18, 2002, March 6, 2002, May 1, 2002, June 7, 2002, November 4, 2002, June 23, 2003. Applicants and the undersigned attorney recognize their duty of disclosure under 37 C.F.R. §1.56 and submit and have

submitted the aforementioned Information Disclosure Statements in accordance with that duty.

Applicants note that the inventors of Peach et al. (WO 98/33513) and the inventors of the instant application are one in the same. Thus there is no reason to hypothesize based on Peach et al. (WO 98/33513) that another inventive entity independently produced the claimed invention before the priority dates of the instant application.

Applicants also note that there is no ATCC deposit associated with the invention of Peach et al. (WO 98/33513).

If the Office remains concerned that the claimed invention may have been publicly available before the priority dates of the instant application, Applicants respectfully request that the Office clearly raise and explain its concerns in a *prima facie,* non-final rejection. Applicants respectfully assert that any such rejection is new and must be non-final. It is not properly brought over Peach et al. (WO 98/33513) as evidenced by Cohen et al. (US 2003/0083246) because the cited references do not state or suggest that the claimed invention was publicly available before the priority dates of the instant application.

Similarly, if the Office believes that more is required of Applicants than acting in accordance with the duty under 37 C.F.R. §1.56, Applicants respectfully request that the Office clearly explain what is required and cite the relevant statutory, regulatory and/or M.P.E.P. provisions(s) that impose any such requirement.

Based upon the foregoing and the arguments previously made in Applicants' responses dated June 1, 2004 and November 29, 2004, Applicants assert that the pending claims are not anticipated under 35 USC 102(b) by the cited references.

Conclusion

Applicants respectfully request that the Patent Office withdraw the rejections under 35 U.S.C. 102(b).

The Examiner is invited to contact the undersigned if there are any questions relating to the prosecution of this application.

The Commissioner is authorized to charge Deposit Account 19-3880 (Bristol-Myers Squibb Company) for any requisite fees due or to credit any overpayment.

Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
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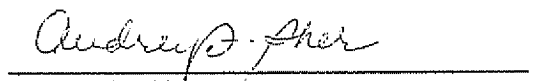

Audrey F. Sher
Attorney for Applicant
Reg. No. 39,024

Date: October 21, 2005

Appendix C -

Notice of Non-Compliant Amendment

D0028 - US - NP

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/865,321	05/23/2001	Robert J. Peach	D0028PNP;30436.57USU1	2959

26941 7590 11/14/2005

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PASADENA, CA 91101

EXAMINER	
OUSPENSKI, ILIA I	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

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Notice of Non-Compliant Amendment (37 CFR 1.121)

The amendment document filed on 10-24-05 is considered non-compliant because it has failed to meet the requirements of 37 CFR 1.121. In order for the amendment document to be compliant, correction of the following item(s) is required. **Only the *corrected section of the non-compliant amendment document* must be resubmitted (in its entirety), e.g., the entire "Amendments to the claims" section of applicant's amendment document must be re-submitted.** 37 CFR 1.121(h).

THE FOLLOWING CHECKED (X) ITEM(S) CAUSE THE AMENDMENT DOCUMENT TO BE NON-COMPLIANT:

☐ 1. Amendments to the specification:
- ☐ A. Amended paragraph(s) do not include markings.
- ☐ B. New paragraph(s) should not be underlined.
- ☐ C. Other_____

☐ 2. Abstract:
- ☐ A. Not presented on a separate sheet. 37 CFR 1.72.
- ☐ B. Other_____

☐ 3. Amendments to the drawings: _____

☑ 4. Amendments to the claims:
- ☐ A. A complete listing of all of the claims is not present.
- ☐ B. The listing of claims does not include the text of all pending claims (including withdrawn claims)
- ☐ C. Each claim has not been provided with the proper status identifier, and as such, the individual status of each claim cannot be identified. Note: the status of every claim must be indicated after its claim number by using one of the following 7 status identifiers: (Original), (Currently amended), (Canceled), (Withdrawn), (Previously presented), (New) and (Not entered).
- ☐ D. The claims of this amendment paper have not been presented in ascending numerical order.
- ☑ E. Other: multiple dependent claims can not depend on other multiple dependent claims. # 74, 96, 116, 114, 117, & 118

For further explanation of the amendment format required by 37 CFR 1.121, see MPEP Sec. 714 and the USPTO website at http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/officeflyer.pdf.

If the non-compliant amendment is a **PRELIMINARY AMENDMENT**, applicant is given ONE MONTH from the mail date of this letter to supply the corrected section which complies with 37 CFR 1.121. Failure to comply with 37 CFR 1.121 will result in non-entry of the preliminary amendment and examination on the merits will commence without consideration of the proposed changes in the preliminary amendment(s). This notice is not an action under 35 U.S.C. 132, and **this ONE MONTH time limit is not extendable.**

If the non-compliant amendment is a reply to a **NON-FINAL OFFICE ACTION (including a submission for an RCE)**, and since the amendment appears to be a *bona fide* attempt to be a reply (37 CFR 1.135(c)), applicant is given a TIME PERIOD of ONE MONTH from the mailing of this notice within which to re-submit the corrected section which complies with 37 CFR 1.121 in order to avoid abandonment. **EXTENSIONS OF THIS TIME PERIOD ARE AVAILABLE UNDER 37 CFR 1.136(a).**

If the amendment is a reply to a **FINAL REJECTION,** this form may be an attachment to an Advisory Action. **The period for response to a final rejection continues to run from the date set in the final rejection**, and is not affected by the non-compliant status of the amendment.

Linda Humes 571-272-0530

Legal Instruments Examiner (LIE) Telephone No.